



Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

JUN 7 - 2004

Mr. Robert C. Bruce  
Chief Operating Officer  
Enterix, Inc.  
236 Fernwood Avenue  
Edison, NJ 08837

Re: K002457  
Trade/Device Name: InSure™ Fecal Occult Blood Test  
Regulation Number: 21 CFR 864.6550  
Regulation Name: Occult Blood Test  
Regulatory Class: II  
Product Code: KHE  
Dated: November 16, 2000  
Received: November 20, 2000

Dear Mr. Bruce:

This letter corrects our substantially equivalent letter of January 12, 2001, regarding the InSure™ Fecal Occult Blood Test. We are correcting the Indication for Use form, which failed to acknowledge by check mark that the sample collection kit is intended for Over-the-Counter distribution. A corrected Indications for Use form is attached to this letter.

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

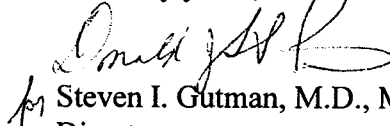
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to continue marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address <http://www.fda.gov/cdrh/dsma/dsmamain.html>.

Sincerely yours,



Steven I. Gutman, M.D., M.B.A.

Director

Office of In Vitro Device Evaluation and Safety  
Center for Devices and Radiological Health

Enclosure

Page 1 of 1510(k) Number (if known): K002457Device Name: InSure™ Fecal OccultBlood Test**Indications For Use:**

InSure™ FOBT is an immunochromatographic fecal occult blood test that detects human hemoglobin from blood in fecal samples. The samples will generally be collected by the test subject at home and the test developed at laboratories or professional offices. The InSure™ FOBT sample collection kit, consisting of a) Test Kit Envelope, b) Instructions for Use, c) Test Card, d) Brush Kit, e) Reply Form, f) Return Envelope, and g) Screening for Life brochure, is intended for Over-The-Counter distribution. Fecal occult blood tests are useful screening aids for detecting primarily lower gastrointestinal (g.i.) disorders that may be related to iron deficiency anemia, diverticulitis, ulcerative colitis, polyps, adenomas, colorectal cancers or other g.i. lesions that can bleed. InSure™ FOBT is recommended for use by health professionals as part of routine physical examinations and in screening for colorectal cancer or other sources of lower g.i. bleeding.

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

  
Division Sign-OffOffice of In Vitro Diagnostic  
Device Evaluation and Safety510(k) K002457Prescription Use ☒  
(Per 21 CFR 801.109)

OR

Over-The-Counter Use ☒*fecal occult blood test*

(Optional Format 1-2-96)

*sample collection kit*

JAN 12 2001

## APPENDIX B

## 510(k) SUMMARY OF SAFETY AND EFFECTIVENESS

**!nSure™ FOBT Immunochemical Fecal Occult Blood Test**

This 510(k) summary of safety and effectiveness information is being submitted in accordance with the requirements of C.F.R. § 807.92

Manufacturer: Enterix Inc.  
348 U.S. Route One  
Falmouth, Maine USA 04105  
Attention: Robert C. Bruce


Proprietary Name: **!nSure™ FOBT**

Classification Name: Occult Blood Reagent

Intended Use: !nSure™ FOBT is an immunochromatographic fecal occult blood test that detects human hemoglobin from blood in fecal samples. The samples will generally be collected by the test subject at home and the test developed at laboratories or professional offices. The !nSure™ FOBT sample collection kit, consisting of a) Test Kit Envelope, b) Instructions for Use, c) Test Card, d) Brush Kit, e) Reply Form, f) Return Envelope, and g) Screening for Life brochure, is intended for Over-The-Counter distribution. Fecal occult blood tests are useful screening aids for detecting primarily lower gastrointestinal (g.i.) disorders that may be related to iron deficiency anemia, diverticulitis, ulcerative colitis, polyps, adenomas, colorectal cancers or other g.i. lesions that can bleed. !nSure™ FOBT is recommended for use by health professionals as part of routine physical examinations and in screening for colorectal cancer or other sources of lower g.i. bleeding.

Predicate Product: *FlexSure® OBT* Immunochemical Fecal Occult Blood Test and, where applicable, Hemocult® SENSEA®. Both tests are manufactured by Beckman Coulter Primary Care Diagnostics, 1050 Page Mill Rd., Palo Alto, CA 94303-0105.

Performance Summary: !nSure™ FOBT is substantially equivalent to the predicate device *FlexSure® OBT*. The performance of !nSure™ was verified by sensitivity, specificity, cross reactivity, interference, reproducibility and readability studies in laboratory and clinical settings. Refer to the attached PERFORMANCE CHARACTERISTICS.



Robert C. Bruce  
Chief Operating Officer  
Enterix Inc.

30 Nov 2000

Date

## **510(k) SUMMARY OF SAFETY AND EFFECTIVENESS**

### **!nSure™ FOBT Immunochemical Fecal Occult Blood Test**

#### **PERFORMANCE CHARACTERISTICS**

##### **Background:**

Fecal occult blood testing (FOBT) is used as a screening aid to detect gastrointestinal (g.i.) bleeding disorders. Three international studies have shown that screening with FOBTs for g.i. bleeding can lead to a significant reduction in deaths from colorectal cancers by the early detection of colorectal neoplasia.

##### **Analytical Performance Studies**

###### **ANALYTICAL SENSITIVITY**

###### **Lower Sensitivity Limit**

*In vitro* studies demonstrated that by following the recommended procedures for sample collection and storage, !nSure™ FOBT reliably detected 50 µg Hb/g feces.

Studies with hemoglobin (Hb) variants HbS (homozygous) and HbE (heterozygous) indicated that !nSure™ FOBT was similarly as sensitive to these forms of hemoglobin as to normal hemoglobin. No other hemoglobinopathies were tested.

###### **Prozone Effect**

*In vitro* studies demonstrated that !nSure™ FOBT reliably detected up to 21 ml of added blood per 100 g of feces (30 mg hemoglobin per g of stool). At this level the blood is generally visible.

###### **ACCURACY OF THE TEST RESULTS**

###### **Cross Reactivity**

!nSure™ FOBT was examined *in vitro* by adding samples of meat extract (myoglobin and hemoglobin) from beef, chicken, fish, horse, pig, rabbit, deer, sheep and kangaroo to the Test Card to determine whether meat extracts cross-react with the test. The samples were added with and without diluted human blood and the cards dried overnight. !nSure™ FOBT gave negative test results when tested with all of the extracts, but was positive in all cases when human blood was present. The meat extracts, when added to a guaiac FOBT (Hemoccult® SENSAR®), consistently gave false-positive results.

## **Interference/Effect of Dietary Substances**

!nSure™ FOBT does not require the patient to follow any special dietary restrictions. Aqueous extracts of raw broccoli, cantaloupe, cauliflower, horseradish, red radish and turnip were added to the Test Card to determine if vegetable extracts cross react with the test. Test cards were also prepared using 20 mg/ml solution of horseradish peroxidase. The extracts were added with and without diluted human blood and dried overnight. !nSure™ FOBT gave negative test results when tested with all of the extracts, but was positive in all cases when human blood was present. The same substances when added to a guaiac FOBT (Hemocult® SENSEA®), consistently gave false-positive results.

An iron supplement and Vitamin C did not interfere with the !nSure™ FOBT performance.

## **Interference by toilet water additives and contaminants**

No evidence was found that any of the toilet bowl deodorizers/fresheners or cleaners studied caused false positive test results. The effect of the products on the sensitivity of the test varied. Some decreased the sensitivity of the test by over four-fold, while others appeared to have no effect. The effects that were noted did not appear to correlate with the noted formulation of the deodorizer/freshener. Based on these studies it is concluded that the labeling for !nSure™ FOBT should be adhered to and that these products should be removed from the toilet bowl prior to collecting samples with !nSure™ FOBT.

A study to assess the effect of residual blood, left in the toilet bowl by an earlier user, showed that provided the !nSure™ FOBT Instructions were followed and the toilet flushed before use, there was no effect on the accuracy of the test.

A 1:1 dilution of urine appears to increase the sensitivity of the test.

Variations in ion concentrations in the toilet bowl water affected the test. This test should not be done if the toilet contains ocean water (high salt content) or rusty (brown) water.

## ***In Vitro* Limits of Detection and Sample Stability,**

Fresh whole fecal specimens were divided into approximately equal aliquots and spiked with whole human blood to concentrations of 0, 10, 30, 50, 100, 200, 500, 1000 and 1500 µg Hb/g feces. !nSure™ FOBT Test Cards were prepared by the standard collection methods. All test cards were stored at room temperature (15-25°C) and tested at 1, 7, 10 and 14 days post preparation. All test cards were read by two experienced, independent readers in a blinded fashion.

Test sensitivity is expressed as the lowest Hb concentration, in ug Hb/g feces, resulting in at least 95% positive readings.

***InSure™ FOBT sensitivity:***

Day 14 = 50 ug Hb/g feces

**Inter-reader Variation and Test Accuracy**

A single stool sample was spiked with whole blood to give hemoglobin concentrations of:

- Negative = 0 µg Hb/g/feces
- Low positive = 10 µg Hb/g/feces *InSure™* FOBT, 60µg Hb g/feces *FlexSure®* OBT
- Medium positive = 30 µg Hb/g/feces *InSure™* FOBT, 200µg Hb g/feces *FlexSure®* OBT

Thirty test cards for each FOBT for each aliquot were tested 24 hours post preparation. All test cards were read by three independent readers in a blinded fashion. The table shows the number of test cards correctly read by each reader.

	<i>InSure™</i> FOBT			<i>FlexSure®</i> OBT		
Reader	A	B	C	A	B	C
Unspiked (n=30)	30	29	30	29	29	28
Low Positive (n=30)	30	30	29	28	30	30
Medium Positive (n=30)	30	30	30	29	28	30
Disagreements (%)	2.2 (2/90)			5.6 (5/90)		
Accuracy (%)	99.3 (2/270)			96.7 (9/270)		

## 510(k) SUMMARY OF SAFETY AND EFFECTIVENESS

### **!nSure™ FOBT Immunochemical Fecal Occult Blood Test**

#### **Clinical Performance**

##### **HIGH RISK POPULATION**

##### **Sensitivity**

The performance of !nSure™ FOBT and *FlexSure® OBT* was assessed in a high risk population of 240 individuals with a personal or family history of colorectal cancer and adenomas. No dietary restrictions were required and the samples were collected as advised by the manufacturer's instructions, i.e. two samples per patient for !nSure™ FOBT and three for *FlexSure® OBT*. The study yielded a relative sensitivity for colorectal cancer of 87% (20/23) (67%- 97%, 95% CI.) for !nSure™ FOBT and 91% (21/23) (72% -99%, 95% CI.) for *FlexSure®*. The sensitivity for large adenomas (> 10mm) was 47.4% (9/19) (24.5%-71%, 95% CI.) for !nSure™ FOBT and 52.6% (10/19) (28.9%-75.6%, 95% CI.) for *FlexSure®*. For small adenomas (<10mm), the sensitivity of both tests was 26.7% (4/15) (7.9%-55.1%, 95%CI.). In all cases the differences were not statistically significant.

##### **STUDIES WITH PRESUMED NORMAL SUBJECTS**

##### **Specificity Studies**

- **Target age normal study**

Persons over the age of 50 years, who had been colonoscoped within the past year and judged to be free of any lower g.i. conditions likely to cause bleeding, were tested with !nSure™ FOBT and *FlexSure® OBT*. . No dietary restrictions were required and the samples were collected as advised by the manufacturer's instructions, i.e. two samples per patient for !nSure™ FOBT and three for *FlexSure® OBT*. The specificity of !nSure™ FOBT was 97.7% (88/90) (92.2%-99.7%, 95% CI.) and *FlexSure® OBT* 94.4% (85/90) (87.5%-98.2%, 95% CI.). The differences were not statistically significant.

- **Young normal study**

The apparent specificity of !nSure™ FOBT and *FlexSure® OBT* for lower g.i. pathology using a group of 94 presumed normal young adults was 97.8% (92/94) (92.5%-99.7%, 95% CI.) and 90.4% (85/94) (82.6%-95.5%, 95% CI.) respectively. In this study, !nSure™ FOBT was statistically more specific than *FlexSure® OBT*.

- **Specificity for upper G.I. Bleeding**

Aspirin and other NSAIDS are known to cause upper g.i. bleeding. To determine the effect of upper g.i. bleeding on !nSure™ FOBT, two healthy subjects ingested 20 ml of autologous blood immediately after the blood was obtained. Subjects commenced collecting samples with !nSure™ FOBT one day prior to blood ingestion and continued to collect samples from each bowel movement thereafter, until six post-ingestion samples had been collected.

None of the samples returned by the subjects tested positive by !nSure™ FOBT. As aspirin and other NSAIDS should not cause 20ml of blood loss, these medications are unlikely to interfere with the !nSure™ FOBT test.